Shock

- Acute syndrome ccc by body's inability to deliver adequate oxygen to meet metabolic demands of vital organs and tissues.
- Anaerobic metabolism. Increases in tissue oxygen extraction are unable to compensate for this deficiency in oxygen delivery, leading to progressive lactic acidosis

Epidemiology

- **Multiple organ dysfunction syndrome (MODS)**
  - Any alteration of organ function that requires medical support for maintenance

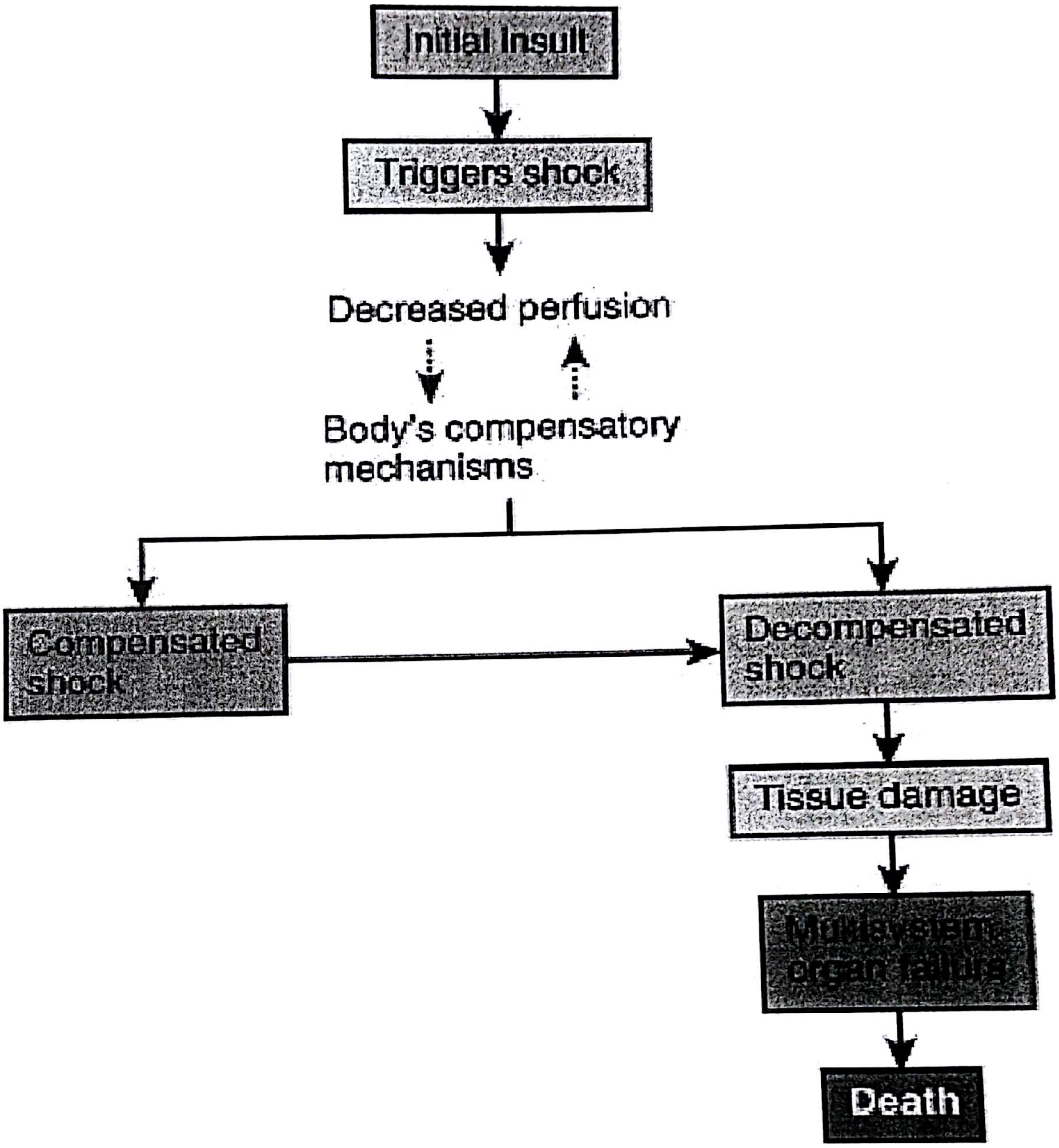
  - **Definition**

TYPES OF SHOCK

HYPOVOLEMIC	CARDIOGENIC	DISTRIBUTIVE	SEPTIC	OBSTRUCTIVE
Decreased preload secondary to internal or external losses	Cardiac pump failure secondary to poor myocardial function	Abnormalities of vasomotor tone due to loss of venous and arterial capacitance	Encompasses multiple forms of shock Hypovolemic: third spacing of fluids into the extracellular, interstitial space Distributive: early shock with decreased afterload Cardiogenic: depression of myocardial function by endotoxins	Decreased cardiac output secondary to direct impediment to right or left heart outflow or restriction of all cardiac chambers
POTENTIAL ETIOLOGIES				
Blood loss: hemorrhage; Plasma loss: burns, nephrotic syndrome;	Congenital heart disease Cardiomyopathies: infectious or acquired, dilated or	Anaphylaxis Neurologic: loss of sympathetic vascular tone secondary to	Bacterial Viral Fungal	Tension pneumothorax Pericardial tamponade

HYPOVOLEMIC	CARDIOGENIC	DISTRIBUTIVE	SEPTIC	OBSTRUCTIVE
Water/electrolyte loss: vomiting, diarrhea	restrictive Ischemia Arrhythmias	spinal cord or brainstem injury Drugs	(immunocompromised patients are at increased risk)	Pulmonary embolism Anterior mediastinal masses Critical coarctation of the aorta

Pathophysiology



- **septic shock** (severe sepsis plus the persistence of hypoperfusion or hypotension despite adequate fluid resuscitation or a requirement for vasoactive agents), **MODS**, and possibly death

INTERNATIONAL CONSENSUS DEFINITIONS FOR PEDIATRIC SEPSIS

Infection	Suspected or proven infection or a clinical syndrome associated with high probability of infection
Systemic inflammatory response syndrome (SIRS)	2 out of 4 criteria, 1 of which must be abnormal temperature or abnormal leukocyte count: 1 Core temperature >38.5°C or <36°C (rectal, bladder, oral, or central catheter) 2 Tachycardia: Mean heart rate >2 SD above normal for age in absence of external stimuli, chronic drugs or painful stimuli *OR* Unexplained persistent elevation over 0.5-4 hr *OR* In children <1 year old, persistent bradycardia over 0.5 hour (mean heart rate <10th percentile for age in absence of vagal stimuli, β-blocker drugs, or congenital heart disease) 3 Respiratory rate >2 SD above normal for age or acute need for mechanical ventilation not related to neuromuscular disease or general anesthesia 4 Leukocyte count elevated or depressed for age (not secondary to chemotherapy) or >10% immature neutrophils
Sepsis	SIRS plus a suspected or proven infection
Severe sepsis	Sepsis plus 1 of the following: 1 Cardiovascular organ dysfunction, defined as:

	• Despite >40 mL/kg of isotonic intravenous fluid in 1 hour:
	• Hypotension <5th percentile for age or systolic blood pressure <2 SD below normal for age *OR*
	• Need for vasoactive drug to maintain blood pressure *OR*
	• 2 of the following:
	    • Unexplained metabolic acidosis: base deficit > 5 mEq/L
	    • Increased arterial lactate: >2 times upper limit of normal
	    • Oliguria: urine output <0.5 mL/kg/hr
	    • Prolonged capillary refill: >5 sec
	    • Core to peripheral temperature gap >3°C
	2 Acute respiratory distress syndrome (ARDS) as defined by the presence of a PaO_2/FIO_2 ratio ≤300 mm Hg, bilateral infiltrates on chest radiograph, and no evidence of left heart failure
	OR
	Sepsis plus 2 or more organ dysfunctions (respiratory, renal, neurologic, hematologic, or hepatic)

Septic shock	Sepsis plus cardiovascular organ dysfunction as defined above
Multiple organ dysfunction syndrome (MODS)	Presence of altered organ function such that homeostasis cannot be maintained without medical intervention

CRITERIA FOR ORGAN DYSFUNCTION

ORGAN SYSTEM	CRITERIA FOR DYSFUNCTION
Cardiovascular	Despite administration of isotonic intravenous fluid bolus ≥60 mL/kg in 1 hour: Decrease in BP (hypotension) <5th percentile for age or systolic BP <2 SD below normal for age *OR* Need for vasoactive drug to maintain BP in normal range (dopamine >5 µg/kg/min or dobutamine, epinephrine, or norepinephrine at any dose) *OR* Two of the following: Unexplained metabolic acidosis: base deficit > 5.0 mEq/L Increased arterial lactate: >2× upper limit of normal Oliguria: urine output <0.5 mL/kg/hr Prolonged capillary refill: >5 sec Core to peripheral temperature gap >3°C
Respiratory	PaO_2/FIO_2 ratio <300 in absence of cyanotic heart disease or pre-existing lung disease *OR* $PaCO_2$ >65 torr or 20 mm Hg over baseline $PaCO_2$ *OR* Proven need for >50% FIO_2 to maintain saturation ≥92% *OR* Need for nonelective invasive or noninvasive mechanical ventilation
Neurologic	GCS score ≤11 *OR*

ORGAN SYSTEM	CRITERIA FOR DYSFUNCTION
	Acute change in mental status with a decrease in GCS score ≥3 points from abnormal baseline
Hematologic	Platelet count <80,000/mm^3 or a decline of 50% in the platelet count from the highest value recorded over the last 3 days (for patients with chronic hematologic or oncologic disorders) *OR* INR >2
Renal	Serum creatinine ≥2× upper limit of normal for age or 2-fold increase in baseline creatinine value
Hepatic	Total bilirubin ≥4 mg/dL (not applicable for newborn) Alanine transaminase level 2× upper limit of normal for age

BP, blood pressure; GCS, Glasgow Coma Scale; INR, International Normalized Ratio; SD, standard deviation.

SIGNS OF DECREASED PERFUSION

ORGAN SYSTEM	↓ PERFUSION	↓↓ PERFUSION	↓↓↓ PERFUSION
Central nervous system	—	Restless, apathetic, anxious	Agitated/confused, stuporous, coma
Respiration	—	↑ Ventilation	↑↑ Ventilation
Metabolism	—	Compensated metabolic acidemia	Uncompensated metabolic acidemia
Gut	—	↓ Motility	Ileus
Kidney	↓ Urine volume	Oliguria (<0.5 mL/kg/hr)	Oliguria/anuria
	↑ Urinary specific		

ORGAN SYSTEM	↓ PERFUSION	↓↓ PERFUSION	↓↓↓ PERFUSION
	gravity		
Skin	Delayed capillary refill	Cool extremities	Mottled, cyanotic, cold extremities
Cardiovascular system	↑ Heart rate	↑↑ Heart rate	↑↑ Heart rate
		↓ Peripheral pulses	↓ Blood pressure, central pulses only

- **Early phases of shock**
  - Multiple compensatory physiologic mechanisms
  - **Increases in**
    - Heart rate
    - Stroke volume
    - Vascular smooth muscle tone
  - Regulated through sympathetic nervous system activation and neurohormonal responses.
  - Increased RR
    - Greater CO_2 elimination
    - Compensatory response to metabolic acidosis
    - Increased CO_2 production from poor tissue perfusion
  - Renal excretion of hydrogen ions and retention of bicarbonate also increase in an effort to maintain normal body pH
  - **Maintenance of intravascular volume:**
    - Facilitated via sodium regulation
    - Renin-angiotensin-aldosterone
    - Atrial natriuretic factor axes
    - Cortisol and catecholamine synthesis and release
    - ADH
- Despite these compensatory mechanisms: vascular endothelial cell injury and significant leakage of intravascular fluids into the interstitial extracellular space.
- **All forms of shock affect cardiac output via several mechanisms**
  - Changes in heart rate
  - Preload, afterload
  - Myocardial contractility

- **Hypovolemic shock**
    - Fluid loss
    - Decreased preload.
    - Tachycardia + increase in systemic vascular resistance initial compensatory responses
    - Without adequate volume replacement, hypotension develops,
    - Followed by tissue ischemia and further clinical deterioration
    - When there is pre-existing low plasma oncotic pressure (due to nephrotic syndrome, malnutrition, hepatic dysfunction, acute severe burns, etc.), even further volume loss and exacerbation of shock

PATHOPHYSIOLOGY OF SHOCK
EXTRACORPOREAL FLUID LOSS
Hypovolemic shock may be due to direct blood loss through hemorrhage or abnormal loss of body fluids (diarrhea, vomiting, burns, diabetes mellitus or insipidus, nephrosis)
LOWERING PLASMA ONCOTIC FORCES
Hypovolemic shock may also result from hypoproteinemia (liver injury, or as a progressive complication of increased capillary permeability)
ABNORMAL VASODILATION
Distributive shock (neurogenic, anaphylaxis, or septic shock) occurs when there is loss of vascular tone—venous, arterial, or both (sympathetic blockade, local substances affecting permeability, acidosis, drug effects, spinal cord transection)
INCREASED VASCULAR PERMEABILITY
Sepsis may change the capillary permeability in the absence of any change in capillary hydrostatic pressure (endotoxins from sepsis, excess histamine release in anaphylaxis)
CARDIAC DYSFUNCTION
Peripheral hypoperfusion may result from any condition that affects the heart's ability to pump blood efficiently (ischemia, acidosis, drugs, constrictive pericarditis, pancreatitis, sepsis)

- **Distributive shock**
  - Abnormal vasodilation
  - Sepsis, hypoxia, poisonings, anaphylaxis, spinal cord injury, or mitochondrial dysfunction
  - lowering of (SVR) is accompanied initially by a maldistribution of blood flow away from vital organs
  - compensatory increase in cardiac output
  - leads to significant decreases in both preload and afterload.

, serum lactate measurements may be used as a marker for the adequacy of oxygen delivery and the effectiveness of therapeutic interventions.

Treatment

Initial Management

GOAL-DIRECTED THERAPY OF ORGAN SYSTEM DYSFUNCTION IN SHOCK

SYSTEM	DISORDERS	GOALS	THERAPIES
Respiratory	Acute respiratory distress syndrome	Prevent/treat: hypoxia and respiratory acidosis	Oxygen
	Respiratory muscle fatigue	Prevent barotrauma	Early endotracheal intubation and mechanical ventilation
	Central apnea	Decrease work of breathing	Positive end-expiratory pressure (PEEP) Permissive hypercapnia High-frequency ventilation Extracorporeal membrane oxygenation (ECMO)
Renal	Prerenal failure Renal failure	Prevent/treat: hypovolemia, hypervolemia, hyperkalemia, metabolic acidosis, hypernatremia/hyponatremia, and hypertension Monitor serum electrolytes	Judicious fluid resuscitation Low-dose dopamine Establishment of normal urine output and blood pressure for age

SYSTEM	DISORDERS	GOALS	THERAPIES
			Furosemide (Lasix) Dialysis, ultrafiltration, hemofiltration
Hematologic	Coagulopathy (disseminated intravascular coagulation)	Prevent/treat: bleeding	Vitamin K Fresh frozen plasma Platelets
	Thrombosis	Prevent/treat: abnormal clotting	Heparinization Activated protein C
Gastrointestinal	Stress ulcers	Prevent/treat: gastric bleeding Avoid aspiration, abdominal distention	Histamine H_2 receptor–blocking agents or proton pump inhibitors Nasogastric tube
	Ileus Bacterial translocation	Avoid mucosal atrophy	Early enteral feedings
Endocrine	Adrenal insufficiency, primary or secondary to chronic steroid therapy	Prevent/treat: adrenal crisis	Stress-dose steroids in patients previously given steroids Physiologic dose for presumed primary insufficiency in sepsis

SYSTEM	DISORDERS	GOALS	THERAPIES
Metabolic	Metabolic acidosis	Correct etiology Normalize pH	Treatment of hypovolemia (fluids), poor cardiac function (fluids, inotropic agents) Improvement of renal acid excretion Low-dose (0.5-2 mEq/kg) sodium bicarbonate if the patient is not showing response, pH < 7.1, and ventilation (CO_2 elimination) is adequate

- Establishment of intravenous (IV) or intraosseous (IO) access
- **Early goal-directed therapy (EGDT)** unless significant concerns for cardiogenic shock
- Rapid IV of 20 mL/kg isotonic saline
- Or less often, colloid should be initiated
- Bolus should be repeated quickly up to 60-80 mL/kg
- .If shock remains refractory"
  - Inotropic therapy (dopamine, norepinephrine, or epinephrine
  - Additional fluids are administered.
  - Current guidelines recommend administration of these inotropic agents via peripheral intravenous (PIV) lines, with very close monitoring of the PIV sites while central venous access is being obtained,
- **Titrated to normalize**
  - Heart rate (according to age-based heart rates)
  - Urine output (to 1 mL/kg/hr)
  - Capillary refill time (to <2 sec)
  - Mental status.
- Fluid resuscitation may sometimes require as much as 200 mL/kg.

Additional Early Considerations

- **Septic shock**
  - Early administration of broad-spectrum antimicrobial
  - **Neonates:**
    - Ampicillin plus cefotaxime and/or gentamicin.
    - Acyclovir: herpes simplex virus
    - Community-acquired infections:
      - *Neisseria 25neumonia25es:* 3rd-generation cephalosporin (ceftriaxone or cefotaxime)
      - Or high-dose penicillin.
  - *Haemophilus 25neumonia:* 3rd-generation cephalosporin (ceftriaxone or cefotaxime).
  - The prevalence of resistant *Streptococcus pneumonia* often requires the addition of vancomycin
- **Distributive shock**
  - Not secondary to sepsis
  - Caused by a primary abnormality in vascular tone.
  - ***Cardiac output*** maintained and may initially be supranormal.
  - Benefit temporarily from volume resuscitation
  - Early initiation of a vasoconstrictive agent to increase SVR is an important element of clinical care.
  - **Spinal cord injury and spinal shock**
    - Phenylephrine
    - Or vasopressin to increase SVR.
    - Epinephrine is the treatment of choice for anaphylaxis

CARDIOVASCULAR DRUG TREATMENT OF SHOCK

DRUG	EFFECT(S)	DOSING RANGE	COMMENT(S)
Dopamine	↑ Cardiac contractility	3-20 μg/kg/min	↑ Risk of arrhythmias at high doses
	Significant peripheral vasoconstriction at >10 μg/kg/min		
Epinephrine	↑ Heart rate and ↑ cardiac contractility	0.05-3.0 μg/kg/min	May ↓ renal perfusion at high doses

DRUG	EFFECT(S)	DOSING RANGE	COMMENT(S)
	Potent vasoconstrictor		↑ Myocardial O_2 consumption Risk of arrhythmia at high doses
Dobutamine	↑ Cardiac contractility Peripheral vasodilator	1-10 µg/kg/min	—
Norepinephrine	Potent vasoconstriction No significant effect on cardiac contractility	0.05-1.5 µg/kg/min	↑ Blood pressure secondary to ↑ systemic vascular resistance ↑ Left ventricular afterload
Phenylephrine	Potent vasoconstriction	0.5-2.0 µg/kg/min	Can cause sudden hypertension ↑ O_2 consumption

- Cardiogenic shock
  - Smaller boluses of fluid (5-10 mL/kg)
  - Dopamine or epinephrine
  - Inodilator, such as milrinone, early in the process.
  - Dobutamine or other vasodilating agents, such as nitroprusside,

VASODILATORS/AFTERLOAD REDUCERS

DRUG	EFFECT(S)	DOSING RANGE	COMMENT(S)
Nitroprusside	Vasodilator (mainly arterial)	0.5-4.0 µg/kg/min	Rapid effect Risk of cyanide toxicity with prolonged use (>96 hours)
Nitroglycerin	Vasodilator (mainly venous)	1.0-20	Rapid effect

DRUG	EFFECT(S)	DOSING RANGE µg/kg/min	COMMENT(S)
			Risk of increased intracranial pressure
Prostaglandin E_1	Vasodilator	0.01-0.2 µg/kg/min	Can lead to hypotension
	Maintains an open ductus arteriosus in the newborn with ductal-dependent congenital heart disease		Risk of apnea
Milrinone	Increased cardiac contractility	Load 50 µg/kg over 15 min	Phosphodiesterase inhibitor—slows cyclic adenosine monophosphate breakdown
	Improves cardiac diastolic function	0.5-1 µg/kg/min	
	Peripheral vasodilation		

- **Obstructive shock**
  - fluid resuscitation
  - Pericardiocentesis for pericardial effusion
  - Pleurocentesis or chest tube placement for pneumothorax,
  - thrombectomy/thrombolysis for pulmonary embolism
  - prostaglandin infusion for ductus-dependent cardiac lesions.
  - **“last drop” or “last straw” phenomenon**
    - Further small amounts of intravascular volume depletion may lead to a rapid deterioration,
    - including cardiac arrest,
- Electrolyte levels
- Hypoglycemia
- Hypocalcemia
- **Hydrocortisone replacement**
  - may be beneficial in pediatric shock.

Considerations for Continued Therapy

- **On the basis of guidelines published in 2009**
    - Hemoglobin should be maintained >10 g/dL
    - $ScvO_2$) >70%,
    - Cardiac index at 3.3-6 L/min/m^2
- **Trials have been conducted**
    - Anti-endotoxin antibodies, antioxidant compounds
    - IL-1 receptor antagonist, IL-1 antibodies
    - Bradykinin receptor antibodies
    - Cyclooxygenase inhibitors, thromboxane antagonists
    - Platelet-activating factor (PAF) antagonists
    - Inhibitors of leukocyte adhesion molecules, nitric oxide antagonists
    - Anti-TNF antibody, bactericidal permeability–increasing protein,
    - Recombinant human activated protein C (drotrecogin-α).
- **If shock remains refractory**
    - **(ECMO)**
    - or a **ventricular assist device (VAD**
- **Prognosis**
- **Septic shock**
    - Mortality rates are as low as 3% in previously healthy children
    - 6-9% in children with chronic illness